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| APPLICATION NO | FILING DATE | FIRST NAME OF INVENTOR | ATTORNEY DOCKET NO | CONFIRMATION NO |
|----------------|-------------|------------------------|--------------------|-----------------|
| 09 529,722     | 04 19 2000  | DAVID J SQUIRRELL      | 124-765            | 3335            |

7590 10 29 2002

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EXAMINER

STEADMAN, DAVID J

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1652

DATE MAILED: 10 29 2002

22

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/529,722

Applicant(s)

SQUIRRELL ET AL.

Examiner

David J. Steadman

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 October 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_ Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_.

3. ☒ Applicant's reply has overcome the following rejection(s): see attached.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s)
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_.

Claim(s) objected to: \_\_\_\_.

Claim(s) rejected: 47-57.

Claim(s) withdrawn from consideration: \_\_\_\_.

8. ☐ The proposed drawing correction filed on \_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_.
10. ☐ Other: \_\_\_\_

**ADVISORY ACTION**

1. Claims 47-57 are pending in the application.
2. Claims 47-57 stand finally rejected.
3. Cancellation of claims 33-46 and addition of claims 47-57 in Paper No. 20, filed 10/02/02, is acknowledged and has been entered.
4. Receipt of a Declaration for Patent Application and a Rule 182 Petition is acknowledged.
5. The request for reconsideration has been considered but does not place the claims in condition for allowance for the reasons discussed below.
6. The objection to the improper grammatical usage of the term "cultures" in claim 34 is withdrawn. The newly added claims appear to properly incorporate the term "cultured".
7. The rejection of claims 33-46 under 35 USC 112, second paragraph, as being indefinite in the recitation of "luciferase remains unaffected", "luciferase is not adversely affected", and "luciferase protein is not adversely affected" is withdrawn. The newly added claims do not appear to recite the language as set forth above.
8. The rejection of claim 42 under 35 USC 112, second paragraph as being indefinite in the recitation of "a luciferase which retains a luciferase activity" is withdrawn. The newly added claims do not appear to recite the language as set forth above.
9. The written description rejection of claims 47-57 under 35 U.S.C. 112, first paragraph, is maintained. Applicants argue the examiner's reliance on *UC California v. Eli Lilly*, (43 USPQ2d 1398) to suggest that the adenylate kinase should be characterized by structural information is inappropriate. Applicants urge the examiner to appreciate that the claimed invention meets the written description requirements, recites specific mutations of the AK in claims 49 and 57 and one of skill in the art would have recognized that applicants' were in possession of the claimed invention at the time of filing. Applicants' argument is not found persuasive. As applicants have not presented particular reasons why the nucleic acid encoding the AK or Luc should not be described by structure, it is unclear to the examiner as to why this rejection is allegedly inappropriate. The court, in *UC California v. Eli Lilly*, (43

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USPQ2d 1398), established that claims to genetic material cannot be described solely by their functional features as is the instant case. It is noted that the limitations of claims 49 and 57, if incorporated into claims 47 and 55, respectively, would appear to provide sufficient structural description of a nucleic acid encoding a mutant AK enzyme. The rejection of claims 47-57 is maintained for the reasons discussed above and for the reasons of record.

10. The scope of enablement rejection of claims 47-57 under 35 U.S.C. 112, first paragraph, is maintained. The examiner can find no written response to the instant rejection in the after final amendment of Paper No. 20. As such, the rejection is maintained for the reasons of record.

11. The rejection of claims 47-57 under 35 U.S.C. 103(a) as being unpatentable over EP 373962 in view of Belinga et al. (J Chromat A 695:33-40), Gilles (Proc Natl Acad Sci, USA 83:5798-5802), and Kajiyama et al. (Biochemistry 32:13795-13799) is maintained. Applicants argue one of ordinary skill in the art would not have attempted to use the method of EP373962 for inactivating AK in the presence of a thermostable Luc because the method of purifying a thermostable enzyme as disclosed by EP373962 uses a mesophilic cell to denature all proteins except the thermostable protein. Applicants argue that based on the teachings of EP373962, one of ordinary skill in the art would not have considered the cell of Gilles suitable for use in a relatively low temperature inactivation of a contaminating protein. Applicants argue the method of EP373962 is used to purify a thermophilic enzyme at temperatures between 65 and 100 degrees Celsius where a majority of the proteins of the host are denatured. Applicants argue that luciferase is not a thermophilic enzyme and the thermostable Luc of Kajiyama is inactivated at a temperature of 65 degrees Celsius. Applicants' argument is not found persuasive. Based on the teachings of Kajiyama, one of ordinary skill in the art would have recognized that the temperatures as disclosed by the method of EP373962 would have inactivated the thermostable Luc. As such, one of ordinary skill in the art would not have applied such extreme temperatures to the Luc of Kajiyama. Instead, temperatures of about 40 degrees Celsius would have been applied to the mutant cell of Gilles expressing a thermosensitive AK and transformed with a vector expressing the thermostable Luc. One of skill in the art would have recognized that it is not necessary to inactivate all proteins by increased temperature – only

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the mutant AK. Motivation to transform the cell of Gilles with a vector expressing a thermostable Luc as described by Kajiyama to practice a method of obtaining Luc free of AK activity would have been provided by Belinga.

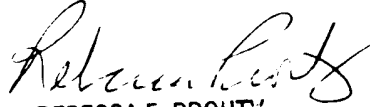
Applicants argue the cited references do not teach or suggest the use of temperatures as low as 37 degrees Celsius. Applicants argue there is no teaching or suggestion that the mutant AK of Gilles is thermosensitive at temperatures as low as 37 degrees Celsius. Applicants' argument is not found persuasive. It is noted that the claims do not recite the limitation of only 37 degrees Celsius. The claims allow for a temperature of AK inactivation of 37 degrees *or more*. As Gilles teaches a mutant AK that is inactivated at a temperature of 40 degrees Celsius, the mutant AK of Gilles would meet the recited limitation.

Applicants argue the cited references would not combine to make obvious the claimed invention absent impermissible use of hindsight. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The cited references combine to teach all limitations of the claimed invention and provide motivation and a reasonable expectation of success for making and using the claimed invention.

The rejection is maintained for the reasons of record and the reasons presented above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

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Patent Examiner  
Art Unit 1652

  
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